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Reply to Cunha et al

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fungal immunity has been demonstrated both in vitro and in vivo [4–6], and there is evidence that the polymorphisms influence the genes' expression [1]. Altogether, these observations make PTX3 polymorphisms a promising host genetic marker of infection in transplant recipients.

Polymorphisms in >20 genes have been reported to influence susceptibility to invasive aspergillosis in oncohematological patients [7]. After initial studies, the concept rapidly emerged that aspergillosis risk could be stratified according to a combination of genetic and nongenetic factors, and that patient management could be personalized, for instance by using specific surveillance and/or prophylactic regimens in the higher-risk patients [8]. Yet, such strategies have not been implemented so far. Some of the polymorphisms initially associated with susceptibility to invasive aspergillosis had low minor allele frequencies [9, 10], thereby limiting the ability to obtain replication, as very large confirmatory cohorts would be needed to reach a sufficient statistical power. Other studies were limited by methodological issues or by a lack of a definite role for the reported genes and/or polymorphism(s) in antifungal immunity [7]. In addition, prophylactic regimens have been used increasingly, especially among hematopoietic stem cell transplant recipients, making it more difficult to replicate associations observed without prophylaxis.

Because the association of *PTX3* polymorphisms seems robust, it might be considered as a key factor for risk stratification. Yet, many questions remain open, such as in which population it would be most beneficial, and to which extent it would impact individual management. Thoracic organ recipients may constitute a potential group for further studies, because those patients have a relatively high risk to develop the infection and they do not routinely receive antifungal prophylaxis in many centers. Yet, due to the small number of patients studied so far, the number of variables that can be implemented together within a potential score

is limited, and makes it difficult to estimate risk and benefit. Large novel prospective studies or meta-analysis from several studies using systematically selected markers would be needed to address these questions before formal recommendations can be made.

Notes

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Agnieszka Wójtowicz,¹ Thanh Doco Lecompte,²
Stéphane Bibert,¹ Oriol Manuel,^{1,3}
Sina Rüeger,^{4,5} Christoph Berger,⁶
Katia Boggian,⁷ Alexia Cusini,⁸
Christian Garzoni,^{8,9} Nina Khanna,¹⁰
Nicolas J. Mueller,¹¹ Pascal R. Meylan,^{1,12}
Manuel Pascual,³ Christian van Delden,² and

Reply to Cunha et al

TO THE EDITOR—In a previous study, Cunha et al showed that polymorphisms in long pentraxin 3 (*PTX3*) influenced susceptibility to invasive aspergillosis among hematopoietic stem cell transplant recipients [1]. A similar association is now reported in 2 studies of solid organ transplant recipients, the Swiss Transplant Cohort Study [2], and a cohort of lung transplant recipients, as described in the current letter by Cunha et al [3]. The risk allele arises, respectively, from the donor of hematopoietic stem cells and from the recipient of solid organ transplant, which is consistent with the different origin of immune cells in these patients. The functional role of *PTX3* in

Pierre-Yves Bochud¹; for the Swiss Transplant Cohort Study

¹Infectious Diseases Service, University Hospital and University of Lausanne, ²Service of Transplantation and Service of Infectious Diseases, University Hospitals of Geneva, ³Transplantation Center, Department of Surgery, ⁴Institute of Social and Preventive Medicine, University Hospital and University of Lausanne, ⁵Swiss Institute of Bioinformatics, Lausanne, ⁶Division of Infectious Diseases and Hospital Epidemiology, University Children's Hospital Zürich, ⁷Division of Infectious Diseases and Hospital Epidemiology, Cantonal Hospital St Gallen, ⁸Department of Infectious Diseases, Inselspital, Bern University Hospital and University of Bern, ⁹Departments of Internal Medicine and Infectious Disease, Clinica Luganese, Lugano, ¹⁰Division of Infectious Diseases and Hospital Epidemiology, University Hospital of Basel, ¹¹Division of Infectious Diseases and Hospital Epidemiology, University Hospital of Zurich, and ¹²Institute of Microbiology, University Hospital and University of Lausanne, Switzerland

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Correspondence: Pierre-Yves Bochud, MD, Infectious Diseases Service, Department of Medicine, Centre Hospitalier Universitaire Vaudois (CHUV), BH 19-105, Rue du Bugnon 46, 1011 Lausanne, Suisse (pierre-yves.bochud@chuv.ch).

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